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## Traumatic subarachnoid haemorrhage

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## 11. SUMMARY

The purpose of this thesis was: 1) to describe the results of a study on the clinical relevance of the finding of tSAH on the initial CT scan after head injury and the significance of the amount and location of blood, and 2) to test in a prospective randomised trial the therapeutical effect of the calcium antagonist nimodipine in tSAH patients.

Additionally some CT scan, demographic and clinical aspects were considered.

These issues were studied in 2 multicentre trials (the European HIT II Study and the German tSAH Study), which analysed nearly four hundred patients with a tSAH visible on CT.

The findings obtained from the analysis of the HIT II study can be summarised as follows:

- tSAH was seen in 33% of the study population.
- The presence of tSAH on the initial CT scan after injury will depend on CT-technical aspects, on the time of performance of the CT-examination, and on age.
- The subarachnoid bleeding due to head injury was highly associated with brain contusions and subdural haematoma.
- tSAH was more frequently observed at the convexity of the cerebral hemispheres than at the basal cisterns.
- Patients with tSAH had an increased incidence of ischaemic brain lesions in follow-up CT scans.
- tSAH represents an important and independent prognostic factor in head injured patients. The presence of tSAH on the initial CT scan after injury worsens significantly the outcome of head injured patients.
- The outcome of tSAH patients depended very closely from the amount and the location of bleeding.
- tSAH patients had an increased incidence of post-traumatic epilepsy.
- The outcome of tSAH patients might be improved with a treatment with the calcium antagonist nimodipine.

A further study (German tSAH study), which objectives were to study the therapeutical effect of nimodipine, as well as some pathophysiological aspects, also addressed some of the evidences listed above.

It was demonstrated:

- tSAH patients have a significant benefit from a therapy with nimodipine. The effect of nimodipine was related to the degree of tSAH as well as to the increase of blood flow velocity (BFV).

Additionally it was shown:

- Increased BFV compatible with vasospasm were observed in up to 30% of tSAH patients.
- The presence of BFV compatible with vasospasm was related to the amount of subarachnoid blood.
- Patients who developed CT scan lesions compatible with ischaemia had a high association with vasospasm according to transcranial Doppler (TCD) criteria.
- The time-course of vasospasm was very similar to that observed in aneurysmal SAH.

The findings listed above are briefly addressed in the following sections.

#### *CT scan aspects*

tSAH was a frequent finding in the head injury population of the HIT II study. One third of patients presented this finding on their first CT scan. It was the second most frequent intracranial finding after brain contusions.

tSAH is an early finding on CT scans after head injury. The detection of tSAH, and the determination of its extent, will depend among others on the morphological changes that have taken place after injury. A rapid swelling of the brain structures or the development of intracranial lesions with mass effect will tend to cause the disappearance of the subarachnoid space.

Most of the patients analysed in the 2 series sustained a small to moderate tSAH. Extensive bleeding was not so frequent, accounting for one quarter of patients in the European study and almost one fifth of patients in the

German series. The most frequent location of bleeding was the convexity of the cerebral hemispheres. Blood was seen at this location in nearly 70% in both series. The basal cisterns were involved in up to 40% of cases. In many cases it was shown that the presence of tSAH forecasts the presence of contusions.

tSAH was associated with a high incidence of cerebral contusions and subdural haematomas, a fact which might indicate the source of bleeding in these patients. Another CT finding which was seen relatively frequent in association with tSAH was blood at the tentorium.

#### *Pathophysiological aspects of tSAH*

Patients in the German study were closely monitored for BFV with TCD. The incidence of unfavourable outcome among those patients who remained within normal BFV limits was relatively low. This changed dramatically when increases of BFV over 80 cm/sec were detected. The worst outcome was seen in those patients who had BFV compatible with vasospasm (mean BFV  $\geq$  120 cm/sec). Almost 30% of patients developed BFV compatible with vasospasm ('vasospasm'). The occurrence of 'vasospasm' was related to the presence of extensive bleeding and to the presence of thick clots as visualised on the first CT scan. The BFV curve in the group of patients who developed a vasospasm showed a very similar shape to that seen in spontaneous SAH, with a peak during the second week after injury.

In regard to secondary ischaemic complications, in the 2 series presented there was a relatively high incidence of hypodense CT lesions compatible with post-traumatic cerebral ischaemia disclosed in the follow-up CT scans. The occurrence of post-traumatic ischaemic lesions was detected in 20% in the European series and 23% in the German series. This complication was seen more frequently in patients with fatal outcome. 'Vasospasm' might be one of the mechanism involved in the development of post-traumatic ischaemia. In this respect it was shown in the German study that the TCD examination is very useful for identifying those tSAH patients who are at higher risk of an unfavourable outcome due to 'vasospasm' and, especially, of developing cerebral ischaemia. This last group of patients were those who most often had an increase in BFV. 'Vasospasm' was detected with TCD in 50% of them.

#### *Demographic and clinical aspects*

There was an increasing frequency of tSAH with age. The mean age was 42 years in the European study and 45 years in the German study. There was a close relation between age and the amount of blood visible on the initial CT after injury.

The presence of alcohol, which has been claimed repeatedly to be related to tSAH was seen in 26% of tSAH in the European trial and in 37% in the German study. It correlated more strongly with tSAH in cases with extensive subarachnoid bleeding.

The occurrence of tSAH was not directly related to the severity of the head injury, as shown by the distribution of initial motor responsiveness in tSAH patients. The German series showed that one quarter of patients had initial Glasgow Coma Scale sumscores of more than 12 points, which corresponds to a mild head injury.

The changes in the values of the various laboratory parameters measured did not differ between tSAH and noSAH patients.

Patients with a tSAH were shown to be at higher risk for hypotensive events and had a higher incidence of episodes of increased intracranial pressure. tSAH patients had an increased incidence of post-traumatic epilepsy, which was twice as common as in noSAH patients. It was observed in 17% of tSAH patients in the European series and in 13% in the German series.

#### **Clinical significance of tSAH.**

*It was postulated that tSAH represents a significant factor determining the outcome of head injured patients. It was also postulated that the outcome will depend from the amount and location of subarachnoid blood.*

Logistic regression analysis showed that tSAH represents an important and independent prognostic factor for outcome in head injured patients, being of a similar degree of importance to the severity of the neurological condition on entry and age. This result is important, since there has been discussion of whether or not tSAH should be thought of as an epiphenomenon of the severity of the head injury.

The greatest impact of tSAH in head injured patients was on mortality, which was 3 times higher than in patients who did not have this CT finding. Unfavourable outcomes (severe disability, vegetative state, dead) were twice as common in tSAH patients at 6-month follow-up than in patients

without this finding. Patients with a tSAH visible on CT scan had an unfavourable outcome in 60% of cases, as shown in the 2 series analysed. The outcome in tSAH patients was also shown to be directly related to the amount of blood seen on the first CT scan and to its location. The amount of blood had the highest predictive value for outcome when compared to factors such as age, severity of the head injury, Fisher's grades, and TCD-BFV among others. The location of the blood, as mentioned before, also influenced the outcome. Patients with blood located mainly at the basal cisterns seemed to have a worse outcome than patients with blood located mainly at the convexity of the cerebral hemispheres. Another aspect that also influenced the outcome of tSAH patients was the thickness of the clot. Patients with thick clots (Fisher's grade 3) had a worse outcome than those with diffuse bleeding and thin clots (Fisher's grade 2).

#### **tSAH and its treatment with nimodipine**

*It was postulated that tSAH patients benefit from a treatment with nimodipine.*

The findings of the HIT II study suggested a beneficial effect of nimodipine in patients with a tSAH visible on CT scan after injury. The German study provided evidence for a significant reduction in unfavourable outcome in tSAH patients treated with nimodipine. Mortality, vegetative state and severe disability were shifted towards a good recovery. The beneficial effect of nimodipine was more accentuated in higher risk patients: those who sustained a moderate to extensive bleeding and those who experienced increase in BFV. Patients treated with nimodipine had a less frequent occurrence of ischaemic lesions visible on follow-up CT scans. This finding underlines a neuroprotective action of nimodipine. With respect to the occurrence of post-traumatic epilepsy, this was reduced in nimodipine-treated patients in both studies. Nimodipine treatment was considered safe and was tolerated well.

The analysis performed in this thesis gave the opportunity to identify tSAH-patients as a well-differentiated subgroup of head injured individuals in regard to pathophysiological, clinical, prognostic and therapeutical aspects.

The recognition of tSAH as an identifiable and separate entity in head injury, suitable of receiving a therapeutic opportunity, may represent a step forward in the management of patients who have suffered a head injury.